UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,410	06/21/2002	Peter Eriksson	59760 (47137)	2145

21874 7590 05/03/2005

EDWARDS & ANGELL, LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
MCGILLEM, LAURA L	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,410	ERIKSSON ET AL.	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01/19/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,9,10,12-15,17,19,21,24-30 and 34* is/are rejected.

7)☒ Claim(s) *2,4-8,11,16,18,20,22,23 and 31-33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Arguments

Claims 1-34 are pending.

Claim Objections

Claims 6, 11, 16, 18, and 33 were objected to as being dependent upon a rejected base claim, specifically claim 1, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The applicants argue that the rejection of claim 1 under 35 USC § 102 (b) is incorrect. However, the applicants are clearly mistaken.

These are new objections necessitated by the filing and acceptance of the terminal disclaimer filed 01/19/2005. Claims 2, 4-5, 7-8, 20, 22-23, and 31-33 are objected to as being dependent upon rejected base claims, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

Claim 30 was rejected under 35 USC 112, second paragraph for the indefinite phrase "such as" which rendered the claimed invention unclear regarding the limitations following the phrase. The Applicants have removed the phrase "such as" and the limitations following the phrase. The rejection is withdrawn.

Claims 30 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 30 recites a method for treating chronic neurodegenerative disease using electrofusion of two fusion partners with cell-like membranes brought into contact with each other. Claim 30 is indefinite because it does not recite how neurodegenerative disease can be treated by electrofusion of two cell-like partners.

Claim 34 recites a method for treating neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease using electrofusion of two fusion partners. Claim 34 is indefinite because it does not recite how Parkinson's disease and Alzheimer's disease can be treated by fusion of two cell-like partners with electrodes.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 9, 10, 13 and 17 have been rejected under 35 U.S.C. 102(b) as being anticipated by Chiu et al (Science, 1999, volume 283, pages 1892-1895). This rejection is maintained for reasons of record in the Office action mailed 10/19/2004 and for reasons which are outlined below. The Applicants argue that the Chiu reference is not properly cited as a 102(b) reference because it was not published more than one year prior to the priority date of the instant application. Applicants' arguments filed 01/19/2005 have been fully considered, but they are not persuasive.

The correct priority date under 35 USC 120, for the instant application is the International filing date of 07/13/2000 and not the foreign application (Sweden 9902817-7) priority date claimed (07/30/1999). Chiu et al. was published 03/19/1999, clearly more than one year prior to the International filing date and prior to the filing date of the foreign application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 9, 10, 13-15, 17 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chiu et al (Science, 1999, vol. 283, pages 1892-1895), in view of Prather et al (US 4,994, 384). The Applicants claim a method for selective electrofusion of at least two fusion partners with cell-like membranes that have been brought into contact with each other prior to electrofusion.

Chiu et al teaches an electrofusion method for fusing lipid vesicles, which reads on cell-like structures using two small electrodes controlled by micromanipulators. The authors teach that the vesicles are provided in a solution and positioned adjacent to each other prior to the electrofusion by optical trapping (abstract, page 1892, figure 1 and column 3, lines 7-24 and page 1893, column 3, lines 9-18, in particular). Chiu et al do not teach the two fusion partners being a cell and a cell-like structure, using electrodes or micropipettes to contact or hold the cell-like structures prior to fusion, treating the fusion partners with electroporation or dielectrophoresis or various applications of electrofusion.

Prather et al disclose using electrofusion for the cloning of an animal (column 3, lines 24-47, in particular) and micromanipulating the cells using a cell-holding pipette with an outer diameter of 120 μm, which reads on a micropipette (column 4, lines 24-29, in particular). Prather et al teach the cell and lipid bound structure situated in a buffer prior to electrofusion by dielectrophoresis using two electrodes. It would have been obvious to one of ordinary skill in the art to modify the teachings of Chiu et al to use

similar manipulation techniques such as electrodes, pipettes and dielectrophoresis prior to electrofusion and to use multiple types of cell-like structures because Chiu et al teach that cell-like structures can be positioned by optical trap prior to electrofusion. Prather et al teach placing a lipid bound vesicle in contact with a cell in a buffered solution before electrically induced fusion. The motivation to do so is the expected benefit as suggested by Chiu et al and actually exemplified by Prather et al of being able to manipulate cell-like structures by various methods prior to electrofusion to joining of the lipid-bound structures. There is a reasonable expectation of success in using electrodes and micropipettes to join adjacent lipid-bound structures by electrofusion for applications such as cloning of non-human mammals since this has worked previously in the cited techniques.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chiu et al, in view of Tanaka et al (US 4,894,343). Chiu et al teach an electrofusion method for fusing lipid vesicles, which reads on cell-like structures using two small electrodes. The authors teach that the vesicles are provided in a solution and positioned adjacent to each other prior to the electrofusion by optical trapping (abstract, page 1892, figure 1 and column 3, lines 7-24 and page 1893, column 3, lines 9-18, in particular). Chiu et al do not teach using electrodes or micropipettes to hold the cell-like structures prior to fusion or pretreatment of the fusion partners with electroporation or dielectrophoresis or various applications of electrofusion.

Tanaka et al disclose that cells are brought into contact with each other prior to the electrofusion of two cells using electrodes (column 4, lines 49-58, in particular).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Chiu et al to use similar manipulation techniques such as application of an electric field with electrodes prior to electrofusion on multiple types of cell-like structures because Chiu et al teach that cell-like structures can be manipulated and positioned prior to electrofusion with optical trapping. Tanaka et al teach that application of high frequency voltage with electrodes can be used to bring cells in contact with each other before fusion. The motivation to do so is the expected benefit as suggested by Chiu et al and actually exemplified by Tanaka et al of being able to manipulate and position lipid-bound structures by various methods such as application of an electric field prior to electrofusion. There is a reasonable expectation of success in using various methods to bring lipid-bound structures in contact before electrofusion since aligning lipid-bound structures before electrical stimulation has improved electrofusion efficiency in the cited techniques.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chui et al in view of Chang et al (US 4,970,154). Chiu et al teach an electrofusion method for joining lipid vesicles, which reads on cell-like structures using two small electrodes. The authors teach that the vesicles are provided in a solution and positioned adjacent to each other prior to the electrofusion by optical trapping (abstract, page 1892, figure 1

and column 3, lines 7-24 and page 1893, column 3, lines 9-18, in particular). Chiu et al do not teach pretreatment of the fusion partners with electroporation or dielectrophoresis or various applications of electrofusion.

Chang et al teaches dielectrophoresis of cells in a solution prior to electrofusion (column 6, lines 48-52 and column 10, lines 50-54, in particular).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Chiu et al to use various manipulation techniques prior to electrofusion on multiple types of cell-like structures because Chiu et al teach that cell-like structures can be positioned by optical trapping prior to electrofusion. Chang et al teaches the use of dielectrophoresis to bring cells in close contact with each other. The motivation to do so is the expected benefit as suggested by Chiu et al and actually exemplified by Chang et al of being able to manipulate lipid-bound structures by various methods such as application of an electric field to bring lipid-bound structures into close contact prior to electrofusion. There is a reasonable expectation of success in using various methods to manipulate cell-like structures such as dielectrophoresis before electrofusion since aligning lipid-bound structures has improved electrofusion efficiency in the cited techniques.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chiu et al in view of Kranz et al (Sex Plant Reproduction, 1991, vol. 4, pages 12-16). Chiu et al

teach an electrofusion method for fusing lipid vesicles, which reads on cell-like structures using two small electrodes. The authors teach that the vesicles are provided in a solution and positioned adjacent to each other prior to the electrofusion by optical trapping (abstract, page 1892, figure 1 and column 3, lines 7-24 and page 1893, column 3, lines 9-18, in particular). Chiu et al do not teach using electrodes or micropipettes to hold the cell-like structures prior to fusion or various applications of electrofusion.

Kranz et al teach the use of electrofusion for the *in vitro* fertilization of single maize sperm cell and a single maize egg cell (abstract, page 13, right column paragraph 1, in particular).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Chiu et al to stimulate adjacent cells or cell-like structures with an electric field to facilitate membrane fusion of cell-like structures because Chiu et al teach that multiple cell-like structures can be brought into close contact and fused by application of electricity using electrodes. Kranz et al teach that similar electrofusion techniques can be applied to single egg and sperm cells of plants for the purposes of *in vitro* fertilization.

The motivation to do so is the expected benefit as suggested by Chiu et al and actually exemplified by Kranz et al of being able to facilitate fertilization of single egg cells with single sperm cells by various electrofusion techniques. There is a reasonable

expectation of success in manipulating cells or cell-like structure to bring them adjacent to each other prior to electrofusion in order to accomplish *in vitro* fertilization of lipid-bound structures since electrofusion has been successfully used for *in vitro* fertilization of maize.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chiu et al in view of Steenbakkers, PGA (US 6,020,170). Chiu et al teach an electrofusion method for fusing cell-like structures using two small electrodes controlled by micromanipulators. The authors teach that the vesicles are provided in a solution and positioned adjacent to each other prior to the electrofusion.

Steenbakkers, PGA discloses the use of electrofusion to produce hybridomas for antibody production (column 3, line 53-58 and column 6, lines 66-67 bridging column 7, lines 1-22, in particular).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Chiu et al to bring cells in close proximity to one another in order to apply an electric field with multiple electrodes to electrically fuse various types of cell-like structures because Chiu et al teach that cell-like structures can be positioned by optical trapping and joined by electrofusion. Steenbakkers, PGA teaches that electrofusion can be used to join B-cell and myeloma cells for the creation of hybridoma cells.

The motivation to do so is the expected benefit as suggested by Chiu et al and actually exemplified by Steenbakkers, PGA of being able to combine cells which have been brought into contact with each other in a buffer and subjected to an electric field sufficient to electrofuse the myeloma and B-cells together in order to generate hybridoma cells. There is a reasonable expectation of success in manipulating cells or cell-like structures to bring them adjacent to each other prior to electrofusion and benefit from the combined properties of both in order to produce antibodies from the resultant hybridoma cells.

Claims 19 and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chiu et al in view of Walker et al (US 6,041,252). Chiu et al teach an electrofusion method for fusing lipid vesicles, which reads on cell-like structures using two small electrodes controlled by micromanipulators. The authors teach that the vesicles are provided in a solution and positioned adjacent to each other prior to the electrofusion by optical trapping (abstract, page 1892, figure 1 and column 3, lines 7-24 and page 1893, column 3, lines 9-18, in particular). Chiu et al do not teach the two fusion partners being a cell and a cell-like structure, using electrodes or micropipettes to contact or holding the cell-like structures prior to fusion, treating the fusion partners with electroporation or dielectrophoresis or various applications of electrofusion.

Walker et al disclose the joining of multiple cells and liposomes by means of electrode stimulation in which the liposome delivers a drug to a cell. For example,

electrofusion is used to deliver drugs to a multicellular tumor, which reads on a treatment for tumors and a cellular network (column 3, lines 16-23 and column 6, lines 43-48, in particular).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Chiu et al to bring lipid-bound structures in close contact with each other prior to electrical induction of lipid membrane fusion because Chiu et al teaches electrofusion of phospholipid vesicles using two small electrodes controlled by micromanipulators. Walker et al disclose the electrically stimulated combination of brain cells and created lipid vesicles which have been designed with components such as specific phospholipid compositions or pharmaceutical compounds. The motivation to do so would be the expected benefit as suggested by Chiu et al and actually exemplified by Walker et al of being able to combine lipid-bound cells or networks of cells and cell-like structures through electrofusion techniques in order to manipulate the composition of the lipid bilayer or facilitate drug delivery to specific tissues for treatment of diseases such as cancerous tumors, There is a reasonable expectation of success in manipulating cells or cell-like structures to bring them adjacent to each other prior to electrofusion in order to introduce the contents of lipid bound structures including pharmaceutically active substance or specific phospholipid compositions from the references cited.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chiu et al. in view of Walters et al (US 6,010,613). Chiu et al teach an electrofusion method for fusing lipid vesicles, which reads on cell-like structures using two small electrodes controlled by micromanipulators. The authors teach that the vesicles are provided in a solution and positioned adjacent to each other prior to the electrofusion by optical trapping (abstract, page 1892, figure 1 and column 3, lines 7-24 and page 1893, column 3, lines 9-18, in particular). Chiu et al do not teach the two fusion partners being a cell and a cell-like structure, using electrodes or micropipettes to contact or holding the cell-like structures prior to fusion, treating the fusion partners with electroporation or dielectrophoresis or various applications of electrofusion.

Walters et al teach using electrofusion to deliver various substances into cells comprising drugs, antibodies, proteins or drugs DNA into cells for cancer therapy (column1, lines 45-47, in particular).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Chiu at al to use manipulation techniques such as electrodes, pipettes and dielectrophoresis on different combinations of cell-like structures prior to electrofusion and to use electrofusion for various applications because Chui et al teaches that lipid-bound structures can be manipulated to direct contact by optical trapping prior to electrofusion of multiple cell-like structures. Walters et al teaches that electrofusion of cells can be used for multiple purposes including introduction of substances into cells.

One would have been motivated to do so by the expected benefit, as suggested by Chiu et al and actually exemplified by Walters of being able to use electrical pulses to fuse lipid cell membranes into order to introduce substances into cells for the treatment of disease including cancer therapy.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chiu et al in view of Heller et al (US 5,827,736). Chiu et al teach a method for fusing cell-like structures using two small electrodes controlled by micromanipulators. The authors teach that the vesicles are provided in a solution and positioned adjacent to each other prior to the electrofusion which joins the two cell-like structures. Chiu et al do not teach the two fusion partners being a cell and a cell-like structure, using electrodes or micropipettes to contact or hold the cell-like structures prior to fusion, treating the fusion partners with electroporation or dielectrophoresis or various applications of electrofusion.

Heller et al teach using electrofusion to join two functionally different cell types in order to a create cell-cell hybrid with characteristic properties of both cells for potential disease therapy (column 3, lines 19-24, column 4, lines 23-27, 31-39 and 54-67, bridging column 5, lines 1-10 and column 6, lines 44-45 and 48-53, in particular).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Chiu et al., to use similar manipulation techniques such as electrodes, pipettes and dielectrophoresis prior to electrofusion and to use multiple types of cell-like structures because Chiu et al teach that cell-like structures can be positioned by optical trapping prior to electrofusion. Heller et al demonstrated that electrofusion could be used to join secretory cells and Sertoli cells to gain the biochemical function of both in the treatment of disease. The motivation to do so to receive the expected benefit as suggested by Chiu et al and actually exemplified by Heller et al of being able to manipulate cell-like structures by various methods prior to electrofusion to accomplish joining of the lipid-bound structures and to use such structures for various applications including treatment of neurodegenerative diseases. There is a reasonable expectation of success in using fusion of cell or cell-like structures for treatment of disease families since electrofusion has worked previously in the cited techniques.

NEW AMENDED CLAIM. It has been noted that Claim 34 was added in response to rejection of the instant claim 30 under the second paragraph of 35 USC § 112. Claim 30 was rejected because the phrase "such as" rendered the limitations that followed the phrase unclear. Claim 30 was amended to delete the phrase "such as" and delete the limitations that followed "such as". The limitations "selected from one or more of Parkinson's disease and Alzheimer's disease" were recited in claim 34 (new).

This is a new rejection necessitated by the Applicants' amendment of claim 30 in the response filed 01/19/2005. Instant claim 34 is rejected as unpatentable over Chui et al., in view of Heller et al (US 5,827,736).

Chiu et al teach an electrofusion method for fusing cell-like structures using two small electrodes controlled by micromanipulators. The authors teach that the vesicles are provided in a solution and positioned adjacent to each other prior to the electrofusion.

Heller et al teach using electrofusion to join two functionally different cell types in order to a create cell-cell hybrid with characteristic properties of both cells for potential disease therapy including neurodegenerative disorders (column 3, lines 19-24, column 4, lines 23-27, 31-39 and 54-67, bridging column 5, lines 1-10 and column 6, lines 44-45 and 48-53, in particular).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Chiu et al., to use similar manipulation techniques such as electrodes, pipettes and dielectrophoresis prior to electrofusion and to use multiple types of cell-like structures because Chiu et al teach that cell-like structures can be positioned by optical trapping prior to electrofusion. Heller et al demonstrated that electrofusion could be used to join secretory cells and Sertoli cells to gain the biochemical function of both. The motivation to do so to receive the expected benefit as suggested by Chiu et al and

actually exemplified by Heller et al of being able to manipulate cell-like structures by various methods prior to electrofusion to accomplish joining of the lipid-bound structures and to use such structures for various applications including treatment of neurodegenerative diseases. There is a reasonable expectation of success in using fusion of cell or cell-like structures for neurodegenerative diseases including Parkinson's disease and Alzheimer's disease since electrofusion has worked previously in the cited techniques.

Double Patenting

The terminal disclaimer filed on 01/19/2005 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 11/30/2001 has been reviewed and is accepted. The terminal disclaimer has been recorded. The provisional obviousness-type double patenting rejections of claims 1-5, 7-10, 12, 15, 17, 21-28 and 31-32 have been withdrawn.

Claims 2, 4-5, 7-8, 20, 22-23, and 31-33 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LLM 4/29/05

DAVID GUZO
PRIMARY EXAMINER